

CLAIMS

1. A chimeric protein, which chimeric protein comprises a Flt3 ligand, or a biologically active fragment thereof, and a proteinous or peptidyl tumoricidal agent.
2. The chimeric protein of claim 1, wherein the tumoricidal agent induces apoptosis.
3. The chimeric protein of claim 1, wherein the Flt3 ligand, or a biologically active fragment thereof, stimulates the proliferation of hematopoietic stem or progenitor cells.
4. The chimeric protein of claim 1, wherein the Flt3 ligand, or a biologically active fragment thereof, stimulates the proliferation of cells selected from the group consisting of myeloid precursor cells, monocytic cells, macrophages, B-cells, dendritic cells and NK cells.
5. The chimeric protein of claim 1, wherein the Flt3 ligand, or a biologically active fragment thereof, is a mammalian Flt3-ligand.
6. The chimeric protein of claim 1, wherein the mammalian Flt3 ligand, or a biologically active fragment thereof, is a human Flt3 ligand.
7. The chimeric protein of claim 1, wherein the Flt3 ligand, or a biologically active fragment thereof, is a soluble Flt3 ligand.
8. The chimeric protein of claim 1, wherein the Flt3 ligand comprises at least 100 amino acid residues and the Flt3 ligand has at least 40% identity to the amino acid sequence set forth in SEQ ID NO:2, in which the percentage identity is determined over an amino acid sequence of identical size to the amino acid

sequence set forth in SEQ ID NO:2, and the Flt3 ligand substantially retains its biological activity.

9. The chimeric protein of claim 1, wherein the Flt3 ligand binds to an antibody that specifically binds to an amino acid sequence set forth in SEQ ID NO:2 and the Flt3 ligand substantially retains its biological activity.

10. The chimeric protein of claim 1, wherein the Flt3 ligand comprises the amino acid sequence set forth in SEQ ID NO:2.

11. The chimeric protein of claim 1, wherein the Flt3 ligand comprises an amino acid sequence that is at least 80% identical to amino acids 28 to 128 of SEQ ID NO:2.

12. The chimeric protein of claim 1, wherein the Flt3 ligand comprises amino acids 28 to 128 of SEQ ID NO:2.

13. The chimeric protein of claim 1, wherein the Flt3 ligand comprises an amino acid sequence selected from the group consisting of amino acid residues 28-160 of SEQ ID NO:2, and amino acid residues 28-182 of SEQ ID NO:2.

14. The chimeric protein of claim 1, wherein the tumoricidal agent is an antibody.

15. The chimeric protein of claim 14, wherein the antibody is selected from the group consisting of an intact antibody, a Fab fragment, a Fab' fragment, a F(ab')₂ fragment, a Fv fragment, a diabody, a single-chain antibody and a multi-specific antibody formed from antibody fragments.

16. The chimeric protein of claim 14, wherein the antibody is selected from the group consisting of an anti-p230 antibody, an anti-CD29 antibody, an

anti-Her2 antibody, an anti-Her3 antibody, an anti-Her4 antibody, an anti-EGFR antibody or a biologically active fragment thereof.

17. The chimeric protein of claim 14, wherein the antibody is a human or humanized antibody.

18. The chimeric protein of claim 1, wherein the tumoricidal agent is selected from the group consisting of Fas ligand, TNF, TRAIL, or a biologically active extracellular domain thereof.

19. The chimeric protein of claim 1, wherein the Flt3 ligand is located at the N-terminus of the chimeric protein.

20. The chimeric protein of claim 1, wherein the Flt3 ligand is located at the C-terminus of the chimeric protein.

21. The chimeric protein of claim 1, wherein the Flt3 ligand and the tumoricidal is separated by a linking peptide.

22. The chimeric protein of claim 21, wherein the linking peptide is (Gly₄Ser)₃.

23. The chimeric protein of claim 1, which comprises the amino acid sequence set forth in SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66 or SEQ ID NO:68.

24. An isolated nucleic acid comprising a nucleotide sequence encoding the chimeric protein of claim 1.

25. The nucleic acid of claim 24, which comprises the nucleotide sequence set forth in SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65 or SEQ ID NO:67.

26. An isolated nucleic acid comprising a nucleotide sequence complementary to the nucleotide sequence of claim 24.

27. A vector comprising a nucleotide sequence encoding the chimeric protein of claim 1.

28. The vector of claim 27, which further comprises expression modulation sequence operatively linked to the nucleic acid encoding the Flt3 ligand and the proteinuous or peptidyl tumoricidal agent.

29. A recombinant cell containing the nucleic acid of claim 24.

30. The recombinant cell of claim 29, which is an eukaryotic cell.

31. The recombinant cell of claim 30, which is a CHO, COS, or NSO cell.

32. A method of producing a chimeric protein comprising growing a recombinant cell containing the nucleic acid of claim 24 such that the encoded chimeric protein is expressed by the cell, and recovering the expressed chimeric protein.

33. The method of claim 32, which further comprises isolating and/or purifying the recovered chimeric protein:

34. The product of the method of claim 32.

35. A pharmaceutical composition comprising an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent, and a pharmaceutically acceptable carrier or excipient.

36. A kit comprising an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent, and an instruction means for administering said chimeric protein.

37. A method for treating neoplasm in a mammal, which method comprises administering to a mammal to which such treatment is needed or desirable, an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent.

38. The method of claim 37, wherein the mammal is a human.

39. The method of claim 37, wherein the neoplasm is melanoma, breast cancer or hepatocellular carcinoma.

40. A combination, which combinaiton comprises:
a) an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent; and
b) an effective amount of an anti-neoplasm agent.

41. The combination of claim 40, wherein the anti-neoplasm agent is an agent that treats melanoma, breast cancer or hepatocellular carcinoma.

42. A method for treating neoplasm in a mammal, which method comprises administering to a mammal to which such treatment is needed or desirable, an effective amount of a combination of claim 40.

43. A method for inducing caspase-3 mediated apoptosis in a cell, which method comprises administering to a cell to which such induction is needed or desirable, an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent.

44. The method of claim 43, wherein the cell is a mammalian cell.

45. The method of claim 44, wherein the cell is a mammalian neoplasm cell.

46. The method of claim 43, wherein the cell is contained in a mammal.

47. A vaccine comprising an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent, and an immune response potentiator.

48. A method for eliciting an anti-neoplasm immune response in a mammal, which method comprises administering to a mammal to which such elicitation is needed or desirable, an effective amount of a vaccine of claim 47.

49. A method for producing a tumor-specific lymphocyte, which method comprises administering to a mammal an effective amount of a chimeric protein comprising a Flt3 ligand and a proteinuous or peptidyl tumoricidal agent to generate a tumor-specific lymphocyte, and recovering said generated tumor-specific lymphocyte from said mammal.